"CORRELATION OF PSEUDO CHOLINESTERASE LEVEL WITH CLINICAL ASSESSMENT AND OUTCOME IN ORGANO PHOSPHORUS POISONING"

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DISSERTATION ON

PART II

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CERTIFICATE

This is to certify that this dissertation entitled **"CORRELATION OF PSEUDO CHOLINESTERASE LEVEL WITH CLINICAL ASSESSMENT AND OUTCOME IN ORGANO PHOSPHORUS POISONING"** submitted by **Dr.M.A.MEHRAJ BEEVI,** to the faculty of Department of Medicine, Tirunelveli Medical College.

The Tamil Nadu Dr. MGR Medical University, Chennai in partial fulfillment of the requirement for the award of M.D Degree Branch I (GENERAL MEDICINE), is a bonafide research work carried out by her under our direct supervision and guidance.

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DECLARATION

I solemnly declare that the dissertation titled **"CORRELATION OF PSEUDO CHOLINESTERASE LEVEL WITH CLINICAL ASSESSMENT AND OUTCOME IN ORGANO PHOSPHORUS POISONING"** is done by me at Tirunelveli Medical College Hospital, Tirunelveli. The dissertation is submitted to The Dr.M.G.R. Medical University towards the partial fulfillment of requirements for the award of M.D.Degree (Branch I) in General Medicine.

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INTRODUCTION

Much of the success in the agricultural field in our country is due to the knowledge and use of agricultural insecticides. Their preparations are most popular on one side and on the other side, also take many lives every year, though mostly in rural areas but also to a considerable extent in the urban areas.

In 1976, the World Health Organization (WHO) using data from 19 countries estimated that approximately 5,000,000 cases of acute pesticide poisoning were occurring annually and resulting in 9000 or more deaths. In 1981, the estimate was 7,50,000 cases annually while in 1983, the figure was 2 million of which 4000 were fatal.[1]

It is estimated that in India about 5-6 persons per lakh of population die due to poisoning. The exact incidence of organophosphorus poisoning in India is uncertain due to lack of data / lack of proper reporting.

The commonest types of insecticidal / pesticide poisoning are organophosphorus compounds, chlorinated hydrocarbons, aluminium phosphide, carbamates and pyrethroids.[2]

The organophosphorus compounds may be inhaled or ingested accidentally or intentionally, in industries, trade, agricultural fields or homes.

The German chemist Gerhard Schrader is credited for the discovery of the general chemical structure of anticholinesterase OP compounds, and for the synthesis of the first commercialized OP insecticides. (Bladan, containing TEPP (Tetra ethyl pyrophosphate) as the active ingredient,and for one of the most known,parathion in 1944.Since then hundreds of OP compounds have been made and commercialized worldwide in a variety of formulations[10].

Organophosphorus compounds are antiacetyl cholinesterases which exert their toxicity by interfering with the normal function of acetyl choline, an essential neuro transmitter throughout the autonomic and central nervous system. The manifestations of toxicity are a result of this effect, affecting the patients physiology. The anticholinesterase effects can be evidenced biochemically by suppression in the plasma levels of pseudocholinesterase(PChE) and of red cell cholinesterase(AChE).

Previous studies associating the severity or prognosis of organophosphorus poisoning with estimation of plasma cholinesterase have been contradictory. GOSWAMY R.et al.,[3] in their study concluded that apart from clinical indicators, low plasma cholinesterase levels were of greatest predictive value for respirtory failure in organophosphorus poisoning. However, Aygun D et al.,[4] found that plasma cholinesterase level estimations are useful in diagnosis of organophosphorus poisoning in acute phase, but not with the severity of poisoning. A.Dua et al.,[5] studied 43 patients of organophosphorus poisoning and found that neither the mortality nor the clinical severity correlate with plasma cholinesterase level.

Semir Nouira et al., estimated pseudo cholinesterase level at the time of admission after organo phosphorus poisoning with the aim to determine whether this has got a prognostic value with reference to severity, treatment, and need for ventilation. They found no correlation between pseudo cholinesterase level and organo phosphorus poisoning as per the above assessment.

In view of this, a study was conducted to know the usefulness of estimation of plasma cholinesterase in predicting the prognosis of organophosphorus poisoning patients.

In the present study, the group of organophosphorus poisoning patients admitted to Tirunelveli Medical College Hospital, were assessed clinically as per a standard institutional management protocol along with estimation of plasma cholinesterase.

AIM AND OBJECTIVES

1. To estimate Pseudo cholinesterase enzyme levels at the time of admission in acute organophosphorus poisoning.
2. To determine whether the Pseudo cholinesterase level has a diagnostic significance.
3. To assess whether the Pseudo cholinesterase levels correlate with the severity and outcome of organophosphorus poisoning.

REVIEW OF LITERATURE

ANATOMY & PHYSIOLOGY OF NEUROMUSCULAR JUNCTION

ACETYLCHOLINE:

Acetylcholine (Ach), first synthesized by BAYER in 1867, is a neurotransmitter. It was first recognized as a potent pharmacological substance by HUNT in 1906.

Acetylcholine is produced at

a)Autonomic effector sites innervated by postganglionic parasympathetic fibres.

b)Preganglionic autonomic fibres of sympathetic and parasympathetic ganglion cells and adrenal medulla.

c)Motor end-plates on skeletal muscle

d)Certain synapses in central nervous system

The Ach in the motor nerve terminal is synthesized in the axoplasm from choline and CoA by a process facilitated by the enzyme choline acetyl transferase. The choline necessary for this is derived from Extra Cellular Fluid which is transported into the nerve terminal by a carrier mediated transport system.[6]

Choline + Acetyl-Co A $\xrightarrow{\text{(Choline Acetyl transferase)}}$ **Acetylcholine**

About 20% of Ach in nerve terminal is present as free Ach in the axoplasm, and 80% is contained within the vesicles, each containing about 4-5 x 10^5 molecules of Ach.

Separate pools or stores of Ach exist within the nerve terminal. Most of the Ach (80%) can be released by nerve impulses (the releasable pool), but some cannot (the non-releasable pool or stationary pool). The releasable pool consists of the Ach contained within the vesicles, whereasnon-releasable pool is the Ach of the axoplasm. Releasable pool is often divided into immediately available and the reserve pool.

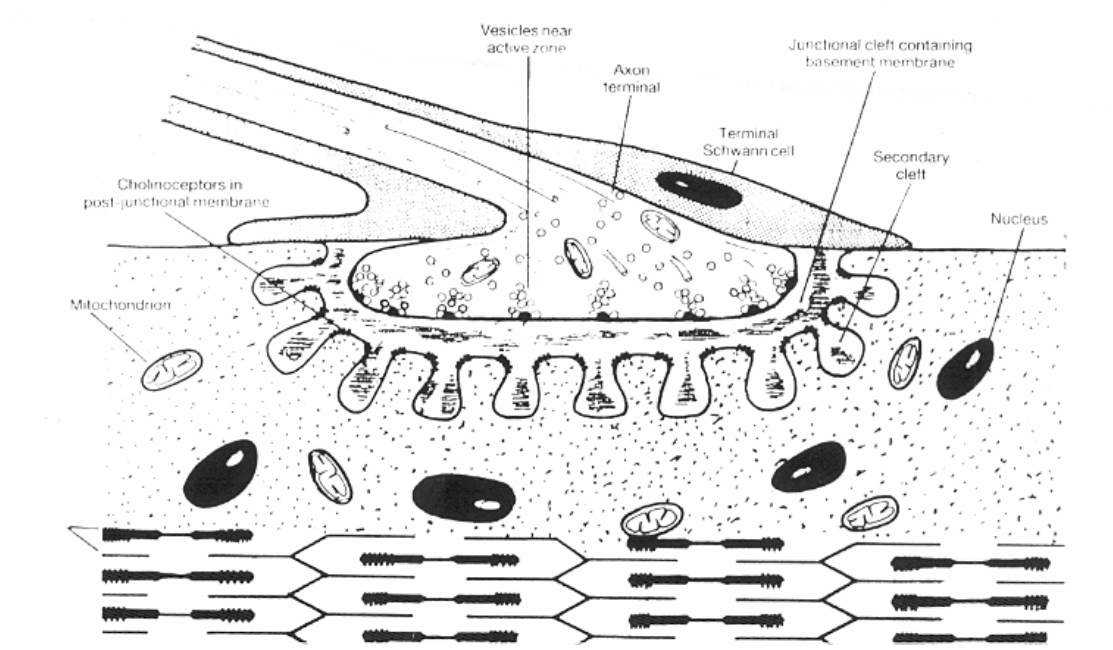
Acetylcholine acts through two receptors:

MUSCARINIC RECEPTORS

Muscarine is a poison from toad stools that activates only muscarinic receptors. Effector cells are stimulated by postganglionic neurons of the parasympathetic nervous system and also postganglionic cholinergic neurons of the sympathetic nervous system.

NICOTINIC RECEPTORS

Nicotine will activate the nicotinic receptors in pre and post ganglionic neurons of both the sympathetic and parasympathetic systems and also in the membranes of skeletal muscle fibres at neuromuscular junction.[6]



Anatomy of Neuromuscular Junction – *The Motor End Plate*[7]

Metabolism of Acetyl choline:

Junctional acetyl cholinesterase is the enzyme responsible for the hydrolysis of Ach in the synaptic cleft.

Acetyl cholinesterase is a protein attached to the basement membrane of the muscle and probably also to membranes of the motor end plates and the nerve terminals. Each molecule of the

enzyme is able to bind and hydrolyze several molecules of acetylcholine. It has been estimated that for each molecule of Ach released by a nerve impulse, there are at least 10 active enzymes sites available. This arrangement ensures that each Ach molecule only reacts once with the receptor, after which it is rapidly (in < 1msec) hydrolyzed.[7]

TYPES OF CHOLINESTERASE:

Two major forms of cholinesterase exist in vertebrates which hydrolyze acetyl choline [8,41]

PLASMA CHOLINESTERASE:(Pseudo or Butyryl Cholinesterase)

It is found in plasma, liver, pancreas and intestinal mucosa. (Liver being the main organ). Variations occur due to liver disease, chronic inflammation, malnutrition, morphine, codeine, succinylcholine administration and hypersensitivity reactions

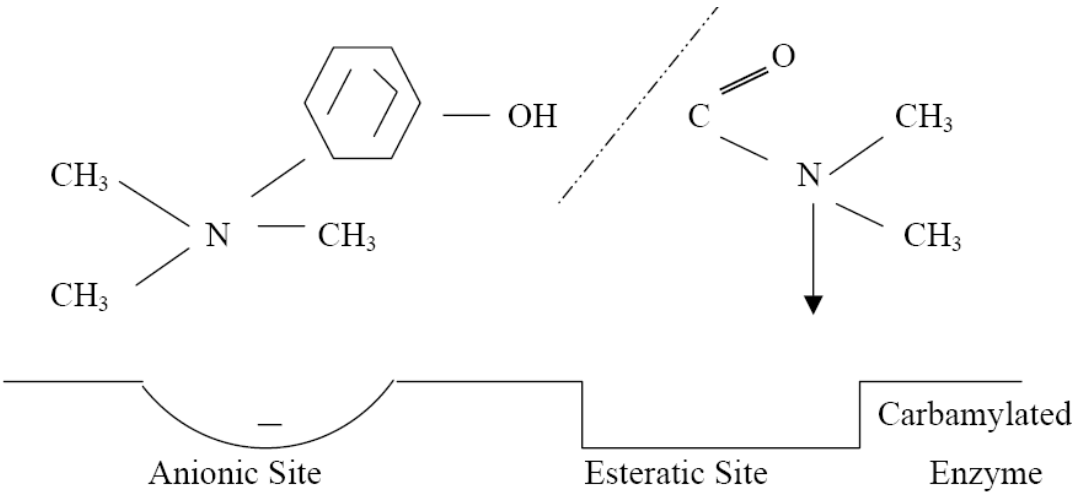
RBC CHOLINESTERASE: (True, Specific Cholinesterase)

It is found in nervous tissue, erythrocytes, Lung, spleen and grey matter. It is decreased in pernicious anemia and after anti-malarial therap.y

Acetylcholine is inactivated by combination with two sites on the enzyme RBC cholinesterase: Anionic site and Esteratic site.

ANIONIC SITE: Bears a negative charge which attracts the quaternary nitrogen ion (N^+) of acetylcholine.

ESTERATIC SITE: Attracts the carboxyl group of Acetylcholine molecule and the esteratic site of the enzyme is acetylated and this results in splitting of choline. The acetyl group in combination with the esteratic site is however immediately removed as a result of combination with water, forming acetic acid. This sets the esteratic site of the enzyme free, for further inactivation of acetylcholine.[9]



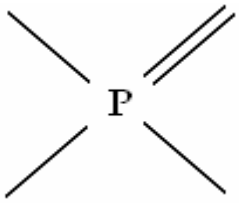
It is the esteratic site (shown above) of the acetylcholinesterase that the organophosphate compounds bind irreversibly to form phosphorylated enzyme.

Chemical structure of organophosphorus compounds:

Although a number of organophosphorus compounds were synthesized in the 1800s, their development as insecticides only occurred in the late 1930s and early 1940s.[10] Since then, hundreds of OP compounds have been made and commercialized world wide in a variety of formulations.

Chemical structure:

The chemistry of Organophosphorus compounds has been thoroughly investigated. The general structure of OP insecticides can be represented by[27]



Where X is the so called "leaving group" that is displaced when the OP phophorylates acetyl cholinesterase (AchE) and is the

most sensitive to hydrolysis. R_1 and R_2 are most commonly alkoxy groups (i.e OCH_3 or OC_2H_5),though other chemical substitutes are also possible; either an oxygen or sulfur are also attached to the phosphorus with a double bond. Based on chemical differences, OPs can be divided into several subclasses, which include phosphates, phosphothioates, phosphoramidates, phosphonates, and others.

Pharmacokinetics:

The kinetics of OPs are highly dependent on multiple physical factors. Some of these include, route of administration (ingestion, injection, inhalation transdermal and transmucosal absorption) distant from target organs, local versus systemic metabolism and activation, route of elimination, endogenous hydrolysis and consumption of the compound by various non specific esterases before reaching target organs. Structural considerations include the groups attached to the sulfur, carbon or phosphorous moiety, the tightness of bond to the central atom and the affinity of the compound for cholinesterase[19].

Onset of symptoms is fastest with inhaled (within seconds) or injected compounds and slowest with transdermal absorption.

The majority of agent should show some signs and symptoms of toxicity within 6 to 12 hours, but highly fat soluble compounds may not manifest toxicity for several days to weeks because the substance must be "bleached out" of the fat until sufficient amount of cholinesterase is inhibited to cause symptoms. Compounds that require hepatic activation to convert the substance to its active toxic state (eg. Parathion to paraxon). Newer data suggests that these residues may remain for days to weeks even after successful treatment of initial symptoms[20].

Mechanism of action:

Traces of acetylcholine are produced at the myoneural junction, which is hydrolyzed to choline and acetic acid spontaneously. Hydrolysis is greatly accelerated by cholinesterase which are present in plasma called pseudocholinesterase and on the membranes or within cytoplasm of many cells including the RBC's called true cholinesterase.[21,22]

Organophosphorus compounds readily react with and inactivate enzymes of cholinesterase type by phosphorylating the enzyme at the myoneural junction and synapses of the ganglion.The toxic effects of organophosphates are due to the

inhibition of acetylcholinesterase, resulting in the excessive accumulation of acetylcholine at the synapse. This initially stimulates and later paralyzes the cholinergic transmission in the CNS,autonomic ganglia,parasympathetic nerve endings,some of the sympathetic nerve endings and neuromuscular junctions.

Mode of action:

Cholinesterase has special reactive sites on its surface, the esteratic site and the anionic site[19]. Acetylcholine is hydrolysed in the following manner.

Electrostatic bond is formed between the quaternary nitrogen on choline and anionic site on the enzyme. This is further strengthened by auxillary bonds between two of the methyl groups on the nitrogen and the surface of the enzyme. Finally a covalent bond is formed between the carbonyl atom of acetate and the esteratic site. Acetylation is rapidly followed by breakage of the ester linkage and the elimination of the choline. Acetylated enzyme then reacts with water to regenerate the enzyme and release acetic acid.

Most of these compounds do not possess a positive charge, hence they react with esteratic site, but not with the anionic site.

Splittering of the acid group then occurs. However the bond between the phosphorus and esteratic site is more stable than the bond between the carbon atom of acetyl choline and the same site. This results in the blocking of the active site and consequent inactivation of enzymes. This results in accumulation of acetyl choline at cholinergic sites and consequent clinical effects. Pseudo cholinesterase is a less specialized enzyme as it lacks an anionic site in a position that specially adapts it to react with acetylcholine. It does, however react with acetylcholine more slowly and also with a wide range of other esters.

Clinical presentation of acute toxicity:

Signs and symptoms of cholinesterase inhibitor poisoning are related to their effects on three separate areas of cholinergic nervous system[19,42].

1. Post ganglionic parasympathetic hollow end organ (muscarinic) effects.
2. Sympathetic and parasympathetic ganglionic and somatic neuromuscular junction (nicotinic) effects.
3. Central nervous system effects.

Muscarinic symptoms noted are as follows;

Tearing,

Drooling of saliva,

Profuse Diaphoresis,

Emesis,

Urinary and fecal incontinence,

Gastro intestinal cramping,

Bronchospasm and Bronchorrhoea,

Miosis, Bradycardia, Hypotension,

Conduction blocks.

Nicotinic symptoms include;

Respiratory difficulty,

Respiratory arrest,

Diaphragmatic weakness,

Muscle weakness, fasciculations,

Clonus, tremor, mydriasis, hypertension,

Tachycardia,

Re entrant dysrhythmia, cardio respiratory arrest,

CNS symptoms include;

Malaise, memory loss, confusion, disorientation, delirium, seizures, coma.

Intermediate syndrome (IMS)

First termed as type II paralysis and subsequently as Intermediate Syndrome(IMS).It occurs 24 to 96 hours after resolution of acute cholinergic crises[26,34]. Clinical features include respiratory failure, bulbar, nuchal and proximal limb muscle weakness. Electromyographic studies show decremental conduction with repetitive nerve stimuli. Recovery is associated with incremental conduction and normalization of Electromyograms. The intermediate and delayed symptoms do not respond to atropine or other drugs[36].

Organophosphate induced delayed neurotoxicity (OPIDN) or polyneuropathy (OPIDP)

It is a sensori motor polyneuropathy that occurs 1 to 3 weeks after exposure to certain organophosphates (disopropyl fluro phosphate, leptophos, diazinon, merphos). The initial toxicity may be mild without the full blown cholinergic presentation. The patient initially complains of distal motor weakness in the lower

extremities and sensory paresthesias. Eventually the patient develops calf cramping and pain. The motor weakness progress to muscle atrophy and paralysis with foot drop. Ataxia develops and the distal tendon reflexes are lost. The neuropathy continues to spread involving upper extremities and eventually develop into a flaccid symmetric paralysis that mimics Guillian Barre syndrome. Some patients may recover over 12 to 15 months, but permanent losses with spasticity and persistent upper motor neuron finding have been reported.[19, 24, 35.]

On a pathological level, the large distal neurons develop axonal degeneration followed by myelin degeneration. This has been called the "Dying back" phenomenon. Degeneration occurs in association with the onset of paralysis and ataxia.

The identified target esterase for OPIDP present in nervous tissues as well as other tissues was named as Neuropathy Target Esterase(NTE)[43.]

Chronic toxicity:

Patients with chronic low level exposure may not show any signs and symptoms until cholinesterase has been inhibited beyond a critical point. The body can maintain normal physiologic

function until cholinesterase activity is inhibited by 20 to 50 percent.[19]

Impairment of pseudo cholinesterase function during chronic exposure to cholinesterase inhibitors also affects levels of medications and toxins that are normally metabolized by pseudo cholinesterase. These include succinylcholine, morphine, codeine, esmolol and local ester anesthetics such as cocaine and tetracaine.

Psychological effects:

Psychological difficulties (Hallucinations, delusions, irritability, nervousness, anxiety, memory loss, depression, dissociation, schizophrenic reactions, behavioral or mood changes) have been reported in a large number of earlier studies related to occupational exposure to agricultural insecticides.[21,24]

Paediatric considerations:

Infants and neonates have lower baseline cholinesterase activity and are at increased risk when exposed to equal amount of organophosphorus compounds. Their under developed, less myelinated nervous system may show additional long term toxicity. Cholinesterase levels are also depressed during pregnancy, especially during the first two trimesters.[19, 25.]

THE ROLE OF ESTIMATION OF PSEUDO CHOLINESTERASE

Estimation of acetyl cholinesterase level in circulation is theoretically preferred in organophosphorus poisoning since it would reflect the degree of inhibition of synaptic cholinesterase at motor end plates. But in practice estimation of plasma cholinesterase has advantage because the measurement is simple and more accurate than estimation of acetyl cholinesterase. Pseudo cholinesterase levels can indicate the prior presence of cholinesterase inhibition even after recovery of acetyl cholinesterase activity by pralidoxime in organophosphorus poisoning.[11]

The normal values range between 5100 to 11700 U/L. According to Proudfoot,[12] the Organophosphorus poisoning may be classified based on the levels of Pseudo cholinesterase (PChE) on presentation as follows :

- *In mild poisoning*: PChE level is 20 - 50 % of normal
- *In moderate poisoning*: : PChE level is 10 - 20 % of normal
- *In severe poisoning*: : PChE level is < 10 % of normal

The confirmation of diagnosis depends on demonstrating reduced cholinesterase activity in the circulating blood.

CHANGES IN ACETYLCHOLINESTERASE LEVELS DURING POISONING AND TREATMENT

- **Plasma cholinesterase inhibition** depends on the concentration of the inhibitor, as this is subject to continuous unknown fluctuations and it is not possible to predict the time course of inhibition. Enzyme inhibition will proceed until a steady state is reached and spontaneous reactivation is achieved.
- **Cholinesterase activity of red blood cells** is instantly and completely restored and long lasting, but the return of activity of pseudo cholinesterase (PChE) is transient and variable after oximes. (The main effect produced by the administration of oximes is the restoration of the true acetylcholinesterase activity & prompt and complete relief of symptoms, especially after alkylphosphate poisoning. True cholinesterase level indicates effectiveness and pseudo cholinesterase levels indicate the prior presence of cholinesterase inhibition. [11]

Diseases as a source of variation on the pseudo cholinesterase activity:

Normal levels are seen in uncomplicated obstructive jaundice, myasthenia gravis, hyperthyroidism, asthma, hypertension, epilepsy and diabetes mellitus.

Low levels are observed in patients with parenchymal liver disease, thiamine malnutrition, etc., In patients with liver disease not only do they have decreased levels but a further decrease ensues as a result of exposure to an organophosphorus compound. Plasma cholinesterase is sharply reduced in acute myocardial infarction and below normal in dermatomyositis. Nephrotic syndrome patients have increased levels of pseudo cholinesterase.[32]

Disadvantages of pseudocholinesterase estimation:

1. Normal values of pseudo cholinesterase are widely variable from one person to another as well as in the same individual at different times.
2. Low pseudo cholinesterase levels have been observed in some disease states and may also be genetically determined.

3. Following pralidoxime administration, true cholinesterase levels indicate the effectiveness of PAM and pseudo cholinesterase levels indicates prior presence of cholinesterase inhibition even after recovery of true cholinesterase activity by PAM, hence the latter cannot be used to assess the effectiveness of PAM therapy.
4. Pseudocholinesterase level at a particular time in the blood is not constant but continuously changing as the inhibition of the enzyme by inhibitors and spontaneous reactivation will take place simultaneously.
5. Different OP compounds may inhibit trueChE or PChE to a different degree.For example the oxygen analogs of malathion,diazinon and chlorpyriphos are stronger inhibitors of PChE than RBC AChE.[29]

Management Of Acute Organophosphorus Poisoning: [8,13]

1. Supportive measures:

Oral suction of secretions

Maintenance of circulation

Establishment of respiration

2. Prevention of absorption:

Decontamination

Emesis

Adsorbant

Cathartics

Bowel wash

3. Specific chemotherapy:

Atropine

Oximes

4.Treatment of complications

1. Supportive measures:

It should be ensured that upper airway is not blocked and throat secretions should be intermittently sucked to avoid aspiration. Respiratory insufficiency is the commonest cause of death. Hence, positive pressure ventilation should be given if patient develops signs of respiratory failure.

2. Prevention of absorption:

a. Decontamination:

Contaminated clothing should be changed, skin should be washed.

b. Emesis:

Unless the patient is comatosed, convulsing or has lost the gag reflex emesis should be initiated. Should these contraindications be present, endotracheal intubation should precede gastric lavage with wide bore tube.

c. Adsorbant:

Activated charcoal functions as an adsorbant and should be given within 3 hours of ingestion and if gastric emptying is delayed it may be useful for upto 12 hours after ingestion. It is the most valuable single agent for emergency management of oral drug poisoning.

d. Cathartics:

Cathartics function by decreasing absorption and increasing elimination. It should be administered as early as possible because relapse is thought to be due to delayed absorption.

e. Bowel wash :

To be done twice a day which helps to remove toxic substance from large bowel.

3. Specific therapy: [1,11]

1. **Atropine**: It is an alkaloid derived from a plant Atropa belladona and Datura stramonium. Atropine acts as a physiological antidote, effectively antagonising the muscarinic receptor- mediated actions of organophosphorus agents. Dose of atropine should be sufficient to produce signs of atropinisation.

Pharmacological action:

At autonomic ganglia where transmission mainly involves nicotinic receptors, atropine produces partial blockade at high doses. Atropine does not inhibit the nicotinic actions of acetylcholine. To some extent it inhibits the central effects produced by these compounds. Thus, atropine antagonises mainly the muscarinic effects of organophosphorus poisoning. Atropine is partially detoxified in the liver and partly excreted unchanged in the kidney.

Dosage:

In order to prevent pulmonary edema, early prompt atropinisation is important. Severe poisoning may require heavy doses, upto 100 mg over first 24 hours to achieve adequate atropinisation. The best clinical approach is, to administer doses of atropine large enough to achieve evidence of atropinisation. Atropinisation should be maintained for at least 48 hours.[28] Higher doses by continuous infusion may be required in severe cases. Overdosage with atropine is rarely serious in OP poisoned patients.[28]

Signs of atropinisation:

Pupillary dilatation cannot be taken as an indication of atropinisation since organophosphorus compounds can produce both miosis or mydriasis. Pupils becoming initially pin point later becoming dilated is a reliable sign of atropinisation. Since tachycardia and bradycardia can occur, tachycardia (130 – 140/min.) cannot be a reliable sign. Other signs include flushing, dry skin and dry mouth. Full atropinisation is indicated by clearing of rales and drying of pulmonary secretions.[14, 26]

Adverse Effects:

Dry mouth, hot dry skin, thirst, flushing, fixed dilated pupil, tachycardia, impaired speech, tremor, coma, convulsions, respiratory failure and collapse.[31, 33.]

2. Oximes:

DOSAGE: Pralidoxime - 1 gm IV followed after 15-30 minutes,by another 1gm if no improvement seen. If no improvement,infusion of 500 mg/ hr can be started.[28]

Obidoxime - 3-6 mg / kg IV over 5-10min.

D.A.M. (Diacetyl Monoxime) -1-2 gm IV slowly at 200 mg / min to be repeated after 20 min.

While animal data consistently show a marked positive effects of oximes some authors reported limited or no efficacy of oximes in the treatment of OP poisoning.[40] Organo phosphates containing two methoxy groups (malathion, methyl parathion, dimethoate) is considered to be rather resistant to oxime therapy.[38] Inadequate dosing has been held as a major factor for lack of response to oxime therapy.[39]

A recent meta-analysis of several studies of OP poisoned patients concluded that use of oximes was associated "with either a null effect or possible hasm".[37]

The IV administration of PAM usually produces *slight to moderate reversal of plasma and red cell cholinesterase inhibition* but has no effect on the gastrointestinal symptoms, tachycardia, sweating, salivation or on CNS symptoms produced by anticholinesterase compounds.

Enzyme reactivation occurs most markedly at the neuromuscular junction with rapid improvement of skeletal muscle response. An important effect of this action is normalisation of diaphragmatic excursion and respiratory effort. To be effective, oximes should be given within 36 hours of poisoning, after which it becomes ineffective by a process called 'ageing'. Phosphorylated cholinesterase undergoes ageing and the aged enzyme is resistant to oxime action and cannot be reactivated.[1,13]

Oximes are effective in severe cases of poisoning presenting with pulmonary edema, muscular twitching, muscle weakness and respiratory paralysis. Prompt recovery of consciousness by many

patients indicate that it has a definitive CNS effect in 10- 15 min. In clinical practice, even 2 or 3 days after onset of poisoning, Oximes might be useful probably because newly inhibited cholinesterase is constantly produced as a result of the continuing absorption of organophosphorus compounds from the GIT or other tissue.

Pralidoxime is preferable since it is more soluble and produces fewer side effects. When given in large doses at the proper time, PAM antagonises the CNS effect of organophosphorus compounds.

Adverse effects:

In higher doses, oximes can inhibit cholinesterase enzyme and they can cause neuromuscular blockade. If infused rapidly they can cause weakness, drowsiness, giddiness, blurred vision, diplopia, headache, nausea, tachycardia and hypotension.Obidoxime can lead to hepatic failure.[26]

3.Treatment Of Complications :

Seizures, Pulmonary edema, Pneumonia, Adult respiratory distress syndrome (ARDS), Renal failure, Hypotension / shock, arrhythmias, etc. are all managed as per standard protocol.[1]

MATERIALS AND METHODS

100 patients with history and clinical features of organophosphorus poisoning admitted to the IMCU of Tirunelveli Medical College hospital between October 2009 to August 2010 were included in this study. Patients were selected irrespective of their age or sex.

INCLUSION CRITERIA for the study were as follows:

1. Provisional diagnosis of organophosphorus poisoning in a patient irrespective of age / sex, based on history by attenders. This was substantiated by examination of the containers.
2. Clinical features suggestive of severe grade of organophosphorus poisoning with clinical evidence of respiratory insufficiency.

EXCLUSION CRITERIA for the study as follows:

1. Patient with double insecticide / multiple poisoning with other drugs such as opioids, diazepam, barbiturate etc.
2. Patients with history of respiratory diseases like bronchial asthma, cardiac diseases, neuromuscular diseases like

myasthenia graves or muscular dystrophy or other concomitant illness.

Each patient enrolled for study underwent a detailed clinical examination as per a proforma, specifically designed for the study. All patients were monitored closely and continuously in the IMCU and all clinical signs assessed ½ hourly till complete recovery. Ventilator support was considered in patients with features of respiratory failure as evidenced by,

- Apnoea or obvious hypoventilation
- Persistent cyanosis.
- Persistent Tachypnoea (RR>24/min)
- Persistent SP O_2 < 90% with oxygen supplementation by non invasive means.
- Active involvement of accessory muscles of respiration.
- All patients underwent baseline biochemical investigations.
- Pseudo cholinesterase levels were estimated at the time of admission.

The blood samples for pseudo cholinesterase estimation were taken along with Anticoagulant heparin or EDTA.

(The kit used in this study for the estimation of pseudo cholinesterase was AGAPPE diagnostics cholinesterase reagent kit)

The pseudo cholinesterase activity was measured by kinetic/DGKC calorimetric method of AGAPPE diagnostics.

The results are expressed in U/L. The laboratory reference range used in the present study for pseudo cholinesterase is 4620-11500U/L

Based on the pseudo cholinesterase values, the severity of poisoning may be defined as per (Proud foot classification)[12] ,with above normal range.

- Mild poisoning PChE level 20 - 50% of normal / >2001 U / L
- Moderate poisoning PChE level 10 – 20% of normal / (1001 – 2000 U/L)
- Severe poisoning : PChE level is <10% of normal / <1000 U/L.

OBSERVATION AND RESULTS

In this present study, the study subjects were analysed according to their demographic characteristics by computing the averages and compared by the test of significance students 't' tests. The study variables and attributes were correlated and associated by correlation coefficients and χ^2 (Chi-square) tests where ever applicable. The above statistical procedure were undertaken by statistical package S.P.S.S (13.0). The value of $P < 0.05$ was treated as significant.

AGE-SEX DISTRIBUTION:

The study subjects were compared according to their age and sex.

Table-1 Age and sex wise distribution of clinical trials.

Age group (years)	Male Patients		Female Patients		Total Patients	
	No.	%	No.	%	No.	%
13-19	8	12.3	5	14.3	13	13.0
20-29	31	47.7	10	28.6	41	41.0
30-39	13	20.0	15	42.8	28	28.0
40-49	7	10.8	3	8.6	10	10.0
50-59	4	6.2	2	5.7	6	6.0
60-69	2	3.0	0	0.0	2	2.0
Total	65	100.0	35	100.0	100.0	100.0
Mean ±S.D	30.4 ±11.3		31.4±10.1		30.7±10.8	
't'	0.438				-	
Significance	d.f = 98 and P>0.05				-	

The study subjects were described according to their demographic characteristics such as age and sex in the above table-1. The male and female proportions were 65% and 35% respectively. The median age with range of age was 27 (16-64) for males. The females median age was 31(17-59) years. The total subjects median age was 29 (16-64) years. The mean age of males and females were 30.4 ±11.3 and 31.4±10.1 years respectively. The mean ages between the sexes was not statistically significant (P>0.05). The mean age of total subjects was 30.7 ± 10.8 years.

TABLE-2 Range of Pseudocholinesterase levels among patients

Range of PChE in U/L	Severity	No of cases	Percentage
<1000	Severe	6	6%
1001 – 2000	Moderate	17	17%
2001 – 3000	Mild	45	45%
3001 – 4000	Mild	21	21%
4001 – 5000	Mild	2	2%
>5000	Normal	9	9%
Mean - PChE		2726.04 ± 1205.377 U / L	
Reference value in this study is 4620 – 11500 U / L			

The above table shows the PChE levels of 100 patients at the time of admission. The mean level in this study was found to be 2726.04 ± 1205.377 U / L in reference to a normal value of 4620 – 11500 U /L. About 89% of patients had a level PChE < 4000 U /L.

Table-3. PChE level among the recovered and expired patients

Outcome	No. of patients	PChE level in U/L		Difference	't' value	d.f	Significance
		Mean	S.D				
Recovered	76	2781.5	1281.1	231.0	0.817	98	P > 0.05
Expired	24	2550.5	927.4				
Total	100	2726.0	1205.4				

The PChE level of recovered patients and expired patients were compared in the above table. Of the total 100 patients studied 76 recovered whereas 24 expired. Recovered group had a mean PChE level of 2781.5 $\pm$ 1281.1 U/L. expired group had a mean PChE level of 2550.5 $\pm$ 927.4. U/L the difference between them was not statistically significant.

Comparision of time delay (consumption to admission) with PChE level.

The time interval taken to admit the patients to the hospital after consumption of poison, was calculated and the same was compared with level of PChE as follows.

Table -4 Comparison of duration of time with PChE level.

Duration of Time(hours)	PChE level in U/L			Total No. of patients	χ^2	d.f	Signi ficance
	< 1000 (Severe)	1000-2000 (moderate)	2000 and above (mild)				
0-2	0	0	2	2	7.902	8	P>0.05
2-4	2	7	15	24			
4-6	2	4	35	41			
6-10	1	5	21	27			
> 10	1	2	3	6			
Total	6	18	76	100			

The PChE level of the patients compared with the time delay was presented in the above table-4. Among the 100 patients, 6 showed severe suppression (<1000 U/L), 18 patients showed moderate suppression (1000-2000) and the remaining showed mild suppression (2000 and above) of PChE according to Proud foot classification.

Among the 6 patients with severe depression of PChE , 2 patients were admitted within 2 - 4 hours, 2patients within 4 – 6 hours, 1 patient within 6 – 10 hours and 1 patient >10 hours after poisoning. The duration of time was not associated with the level of PChE. (P>0.05).

Biochemical profile:

The biochemical statistics such as blood glucose level, urea and creatinine were analysed and the results are as follows.

Table-5 Biochemical profile of the study subjects.

Blood glucose		Urea		Creatinine	
Level (mg/dl)	No of person (frequency)	Level (mg/dl)	No of persons	Level (mg/dl)	No of persons
50-100	23	15-20	1	0.5 - 0.75	1
100-150	63	20-25	56	0.75 – 1.00	30
150-200	13	25-30	26	1.00 – 1.25	65
200 and above	1	30 and above	17	1.25 - 1.5	4
Total	100	Total	100	Total	100
Mean ±S.D	121.1±31.6	25.3±6.4		1.0±0.14	

The related biochemical values were described in the above table-5. The mean blood glucose level was 121.1 ± 31.6 mg/dl. The same of the other two variables namely urea and creatinine were 25.3 ±6.4 and 1.0±0.14 mgm/dl.respectively.

Comparision of PChE level and outcome with route of exposure

Table-6 Comparision of route of exposure with PChE level.

Route of exposure	PChE level U/L			Total No. of patients	χ^2	d.f	Significance
	Severe <1000	Moderate 1000 - 2000	Mild >2000				
Inhalation	1	2	9	12	0.139	2	P>0.05
Oral	5	16	67	88			
Total	6	18	76	100			

The route of exposure was associated with the PChE level in the above table-6. The results of the test of significance revealed that there was no association between the route of exposure and the PChE level (P>0.05).

Table-7 Relation between route of exposure and outcome.

Route of exposure	Expired No. of patients	Recovered No. of patients	Total No. of patients	χ^2	d.f	Significance
Inhalation	4	8	12	0.651	1	P>0.05
Oral	20	68	88			
Total	24	76	100			

The above table-7 explains the relationship between the route of exposure and the outcome of patients. The chi-square value (0.651) at 1 degree of freedom reveals that there was no statistically significant association between the route of exposure and out come (P>0.05)

PChE level and outcome related with symptoms.

The PChE level and outcome of the patients were related with symptoms of patients.

Table -8 Symptoms related with PChE level.

Symptoms	PChE level U/L				χ^2	d.f	Significance
	Severe < 1000	Moderate 1000 - 2000	Mild > 2000	Total No. of patients			
M	4	12	36	52			
M + N	2	5	33	40			
M + N + C	0	1	5	6	3.308	6	P>0.05
N + C	0	0	2	2			
Total	6	18	76	100			

M- muscarinic ; N- nicotinic ; C- central nervous system features

The above table-8 describes the relation between the symptoms and PChE level. The Muscarinic (M) symptoms were found in 52% of patients. The remaining symptoms M+N, M+N+C and N+C were found in 40%, 6% and 2% respectively. The symptoms were not related with PChE level since there was no statistically significant association between them (P>0.05).

Table -9 Symptoms related with outcome.

Symptoms	Expired		Recovered		Total	χ^2	d.f	Significance
	No	%	N o	%				
M	1	4.2	51	67.1	52			
M+N	17	70.8	23	30.3	40			
M+N+C	4	16.7	2	2.6	6	33.722	3	P<0.001
N+C	2	8.3	0	0.0	2			
Total	24	100	76	100	100			

M- muscarinic ; N- nicotinic ; C- central nervous system features

The above table-9 associates the symptoms and outcome of the patients. The muscarinic symptoms were statistically significantly associated with recovered patients, since 67.1% of the recovered patients had only muscarinic symptoms. The symptoms M+N, M+N+C and N+C were statistically associated with expired patients. There was statistically a very highly significant association between the symptoms and outcome (P<0.001).

Respiratory Failure compared with PChE level and outcome

The poisoned patients were compared according to the presence of respiratory failure with PChE level and outcome.

Table -10 Association of respiratory failure with PChE level.

Respiratory failure	PChE level U/L			No.of patients	χ^2	d.f	Significance
	Severe <1000	Moderate 1000 - 2000	Mild >2000				
Yes	2	11	34	47	2.045	2	P>0.05
No	4	7	42	53			
Total	6	18	76	100			

The above table-10 illustrates that the respiratory failure cases were 47%and non respiratory failure cases were 53%. The respiratory failure was not statistically significant with PChE level (P>0.05)

Table -11 Relationship between respiratory failure with the outcome of patients.

Respiratory failure	Expired No. of patients	Recovered No. of patients	Total No. of patients	χ^2	d.f	Significance
Yes	23	24	47	0.5498	100	P<0.001
No	1	52	53			
Total	24	76	100			

The respiratory failure cases were correlated with outcome of patients in the above table-11. Among the expired group the respiratory failure presented in 95.8%(23 out of 24). Only one (4.2%) patient expired among the non respiratory failure cases. The correlation was statistically very highly significant (P<0.001).

Atropine Requirement with PChE level and outcome

The quantity of atropine administered was associated with PChE level and outcome of the patients.

Table -12 Association between atropine requirement with PChE level.

Level of atropine used in mgm	PChE level U/L			Total No. of patients	X^2	d.f	Significance
	Severe <1000	Moderate 1000-2000	Mild >2000				
<100	0	1	5	6	6.759	6	P>0.05
100-200	2	5	42	49			
200-300	3	8	22	33			
300-400	1	4	7	12			
Total	6	18	76	100			

The above table 12 states that the atropine requirements of the patients were not statistically correlated with the PChE level. (P>0.05)

Table –13 Correlation between Atropine requirement and outcome.

Atropine Dosage in mgm	Expired		Recovered		Total	
	N o	%	N o	%	N o	%
<100	0	0.0	6	7.9	6	6.0
100-200	9	37.5	40	52.6	49	49.0
200-300	10	41.7	23	30.3	33	33.0
300-400	5	20.8	7	9.2	12	12.0
Total	24	100	76	100	100	100
Mean ±S.D	231.0 ± 78.0		191.3 ± 77.8		200.8 ± 79.3	
't'	2.170				-	
Significance	d.f = 9 and p<0.05				-	

The atropine administered to the poisoned patients was correlated with the outcome. The mean atropine administered to the expired patients was 231.0 ± 78 mgm and the same administered to the recovered patient was 191.3 ± 77.8 mgm. The difference of mean 39.7 was statistically significant (P<0.05). The relationship between the atropine and outcome was statistically significant (P<0.05).

DISCUSSION

Age sex distribution

In our study it was found that majority of the patients were males (65%). This could be because males have easy accessibility to organophosphorus compounds . Majority of patients (69%) belonged to the age group of 20 -39 years(Mean age – 30.7 ± 10.8years).

Major route of poisoning was by oral ingestion. There was no correlation between route of poisoning and outcome or PChE level.

Nearly 74% of patients were brought after 4hours of poisoning.

This could be related to the fact that majority of patients were from rural areas and needed to be brought to the hospital for management by road.

The mean blood glucose level was 121.1 ± 31.6 mg/dl. The same of the other two variables namely urea and creatinine were 25.3 ±6.4 and 1.0±0.14 mgm/dl respectively.

PSEUDOCHOLINESTERASE LEVEL AT THE TIME OF ADMISSION.

In our study, taking into consideration the lower limit of reference value of PChE, only 9 patients had PChE value of more than 4600 indicating that there was suppression in more than 90% patients on admission.(reference range 4620 – 11500 U/L).

The mean PChE level was **2726.04 ± 1205.377 U/L**

A. Dua et.al.,[5] also found that PChE was lower than normal in all their study patients with OP poisoning .

Suvit areekul et. al., [15] studied 10 patients with OP poisoning and found reduced level of PChE in all of them with one mortality.

In 23 cases of OP poisoning Mehta A.B et al., [16] observed lower activity of PChE in more than 70% of cases at presentation.

Thus reduced level of PChE at the time of admission can raise a strong suspicion of OP poisoning .

RELATIONSHIP BETWEEN MORTALITY AND PChE

There was a mortality rate of 24% in our study with no relation to PChE level.

The mean PChE level of expired group was 2550.5 ± 927.4U/L.

The mean PChE level of recovered group was 2781.5 ± 1281.1U/L.

The difference between the two was not statistically significant.

Mehta.A.B. et al.,[16] reported similar patterns in their study wherein 2 patients with severe suppression (values of < 10% PChE)could survive.

J.Sunder ram et al.,[17] observed a mortality of 8% (4 out of 45) with no correlation with PChE values.

A. Dua et al.,[5] studied 43 patients of OP poisoning and found that neither the mortality nor the clinical severity correlate with PChE level. This indicates that there is no relation between mortality and PChE levels.

TIME DELAY FROM POISONING TO ADMISSION

Only 6 patients were admitted after 10 hrs. Among them only 1patient had severe and 5 patients had mild to moderate suppression,Similarly among the patients showing severe suppression of PChE levels (6%), only one patient was admitted

after 10hrs, 33% of patients were admitted within 4 hrs.Thus there was no relation between the time delay from poisoning to admission and PChE level suppression.This can be explained as the amount of toxin taken is more important than the time delay.

RELATION OF SYMPTOMS WITH PChE LEVELS

Majority of patients(98%) presented with muscarinic features. Of these 52% presented with only muscarinic features and they constitute 67 % of recovered group.

The patients with associated nicotinic features were 48% and they constitutes 96% of expired group.

Thus presence of nicotinic features indicate more chances of mortality.

Among the patients with only muscarinic features (52), severe suppression of PChE levels was seen in 4; moderate suppression in 12; and mild suppression in 36 patients. Among the patients with associated nicotinic features (48), severe suppression in 2; moderate suppression in 6; and mild in 40 patients. Thus there was no correlation between symptoms and PChE levels.

RELATION OF PChE LEVEL WITH RESPIRATORY FAILURE

Respiratory failure cases were 47 in this study. Among them majority (34 out of 47) had only mild PChE level suppression. Among the patients having severe suppression(6), the non respiratory failure cases were 4.Thus there was no significant correlation between PChE level and the presence of respiratory failure.

RELATION OF RESPIRATORY FAILURE AND OUTCOME

Among the expired group of patients, presented with respiratory failure was 95.8% . The relationship between respiratory failure and mortality was highly significant.

Thomas Chang-Yao Tsao et al., [30] found over a five year period that respiratory failure developed in about 40% of organo phosphorus poisoning or carbamate poisoning and half of them died due to respiratory failure.

Semir nouira et al., [14] did not find any statistically significant difference in mean PChE levels in those mechanically ventilated and those not needing ventilator support.

Wadia et al., [18] found no correlation between various clinical signs and levels of RBC Cholinesterase and PChE.

Mehta et al.,[16] also found no correlation between severity of poisoning clinically and PChE levls in their study.

Most of the above studies indicate that there is no correlation between PChE levels and the clinical severity of poisoning, such as presence of respiratory insufficiency. Also PChE levels do not appear to have any prognostic value as far as OP poisoning is concerned.

RELATIONSHIP BETWEEN PChE AND TOTAL DOSE OF ATROPINE REQUIRED

The average dose of atropine required was 250.8 ±79.3mg. Among the 12 patients administered higher doses of atropine (300 – 400mg) , 7 patients showed only mild suppression of PChE level. Thus there was no clear correlation between atropine dosage administered and PChE levels in our study.

RELATIONSHIP BETWEEN OUTCOME AND TOTAL DOSE OF ATROPINE REQUIRED

The mean atropine required in expired patients were significantly higher than that required in recovered patients.Thus higher requirement of atropine in a patient can be taken as a predictor of severity and mortality.

Semir nauira et al., did not find any statistically significant differences in mean PChE levels in those mechanically ventilated and those not needing ventilator support. They found that the total dose of atropine required and the simplified acute physiology score (SAPS) used to grade clinical severity, did not correlate with the PChE values.

CONCLUSION

The present study on pseudo cholinesterase levels in organophosphorous poisoning patients was conducted in 100 patients admitted in Intensive Medical Care Unit of Tirunelveli Medical College Hospital.

1. We found in our study that the patients were predominantly males, between the age group of 20 to 40 years. There was significant association between the presence of nicotinic features or respiratory failure, atropine dose used and outcome of poisoning.
2. In majority of cases, we found suppression of Pseudo cholinesterase level at the time of admission to the hospital, which confirms the diagnosis of organophosphorus poisoning.

However our study did not reveal any relation between

- PChE levels and the time of presentation after poisoning
- PChE levels and respiratory insufficiency
- PChE levels and atropine dose used
- PChE levels and mortality

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PROFORMA

1.Name of the patient :

2.Age :

3.Sex :

4.In Patient Number :

5.Time of exposure of OPC :

6.Route of exposure :

7.History of present illness :

a.Tightness in the chest :

b.Nausea,Vomiting :

c.abdominal cramps :

d.Diarrhoea :

e.Involuntary defecation :

f.Excessive sweating :

g.Exessive salivation :

h.exessive lacrimation :

i.blurring or dimness of vision :

j.involuntary micturition :

k.muscle twitching :

l.respiratory difficulty :

m.irritability :

n.loss of consciousness :

o.convulsions :

G/E

Pulse :

BP :

RR :

Temp :

SYSTEMIC EXAMINATION

CNS

GCS :

	Rt	Lt
PUPIL SIZE :		
SPINO MOTORSYSTEM :		
Deep Tendor Reflexes :		
PLANTAR :		

CVS:

RS:

LAB:

Urine-albumin,sugar,deposit :

Blood TC,DC,HB,ESR :

BLD sugar,urea creatinine,electrolytes:

ECG :

X-RAY Chest PA :

SPO2 :

Pseudo cholinesterase level :

Total dose of Atropine required for treatment:

Outcome :

Sl.No	Age	Sex Male/ Female	IP No.	TIME INTERVAL BETWEEN EXPOSURE TO ADMISSION IN (HOURS)	ROUTE OF EXPOSURE	SYMPTOMS	BLOOD SUGAR IN mgm /dl	BLOOD UREA IN mgm/dl	SERUM CREATINE IN mgm/dl	PSEUDOCHOLINE ESTERASE LEVEL U/L	RESPIRATORY FAILURE	TOTAL AMOUNT OF ATROPINE IN mgm/dl	OUTCOME
1	24	M	48149	8	O	M	138	26	1.2	863	N	252	R
2	35	M	48378	6	O	M	108	20	1	2980	N	180	R
3	39	M	48452	4	O	M+N	60	26	0.9	691	Y	144	E
4	18	F	48502	5	O	M+N	140	30	1.1	2172	Y	192	E
5	28	M	48516	4	I	M	107	24	0.9	2843	N	204	R
6	20	M	48588	5	O	M	124	22	1	3479	N	264	R
7	29	F	48753	2	O	M+N	112	20	1	2988	N	288	R
8	58	F	48788	3	O	M	186	26	1.2	2649	N	156	R
9	22	M	48885	2	O	M	104	22	0.9	1061	N	132	R
10	32	F	48995	8	O	M+N	94	26	1	1760	Y	240	E
11	19	M	48992	4	O	M	108	24	1	1743	Y	348	R
12	21	F	48169	2	O	M+N	96	30	1.2	2824	Y	180	R
13	42	M	49241	6	O	M	120	20	1	4486	N	120	R
14	24	M	49364	4	O	M	126	22	0.9	2678	N	132	R
15	31	F	49601	2	O	M	124	20	1	973	N	216	R
16	30	M	49760	4	O	M	112	26	1	3210	N	180	R
17	18	M	49907	2	O	M	92	24	1	1621	N	264	R
18	43	M	50070	1.5	O	M+N	142	28	1	5249	Y	228	E
19	29	F	50038	9	O	M	98	28	1	1084	N	300	R
20	21	M	50610	5	O	M+N	94	20	1.2	3842	Y	264	R
21	27	F	50872	6	O	M	96	28	1	2960	N	144	R
22	53	M	50908	3	I	M+N	102	26	1	3109	Y	360	E
23	31	F	50990	6	O	M	186	24	1	2761	N	180	R
24	23	M	51085	10	O	N+C	120	20	1.2	2188	Y	264	E
25	33	M	51278	8	I	M	114	32	1.1	1242	N	288	R
26	17	F	51296	10	O	M	94	30	0.9	218	N	120	R
27	38	F	51313	1	O	M	108	22	1	5104	N	144	R
28	28	M	51360	5	O	M+N	112	26	1	3690	Y	276	E
29	19	F	50313	4	O	M	107	24	1.2	2872	N	48	R
30	33	M	51974	5	O	M	124	30	1	3084	N	168	R
31	17	M	52039	6	0	M	102	20	0.9	2622	N	264	R
32	23	M	52047	10	O	M+N	110	22	1.1	1431	Y	108	E

33	39	F	52557	4	O	M	96	26	1	3180	N	144	R
34	28	M	52570	5	O	M	80	24	1	1731	N	348	R
35	32	F	52719	2	O	M+N+C	110	30	1	1018	Y	240	R
36	21	F	53061	5	O	M	124	20	1	3248	N	144	R
37	62	M	53578	5	O	M	107	22	1.4	2212	N	108	E
38	19	M	53732	2	O	M	190	20	1	1914	N	252	R
39	31	F	53964	4	O	M+N	112	26	0.9	3670	Y	144	E
40	25	M	54373	5	I	M+N	142	24	0.8	2649	Y	348	E
41	24	M	54450	3	O	M	108	28	1.2	2977	N	156	R
42	34	F	54446	2	I	M+N	136	40	1	741	Y	360	R
43	17	M	55092	4	O	M	140	24	1	2627	N	168	R
44	27	M	406	5	O	M	60	72	0.9	6246	N	120	R
45	18	M	408	4	O	M+N	92	32	1.1	2193	Y	216	R
46	31	F	649	6	O	M	172	24	0.9	3064	N	120	R
47	43	M	682	6	I	M	116	26	1.4	1267	Y	348	R
48	22	M	1363	8	O	M+N	124	20	1	4827	N	276	R
49	30	F	1508	5	O	M+N	120	24	1.2	2211	Y	132	R
50	20	M	1663	6	O	M+N+C	136	20	1	3182	Y	240	E
51	48	M	1791	4	I	M	112	18	0.9	2173	N	108	R
52	27	M	1823	4	O	M+N	108	28	0.8	5104	Y	168	R
53	24	F	1895	6	O	M+N	126	30	1	3876	N	264	R
54	25	M	2093	10	O	M	132	20	1.1	2198	Y	360	R
55	41	F	2137	2	O	M+N	106	26	1.2	2964	Y	216	E
56	18	F	2201	6	O	M	128	24	1	5082	N	144	R
57	32	M	2254	6	O	M	132	22	1.2	2742	N	300	R
58	23	M	2465	12	O	M+N	90	30	1.2	1434	Y	288	R
59	22	F	2469	3	O	M	96	34	0.9	1765	N	168	R
60	51	M	2577	4	I	M+N	162	26	0.8	2069	Y	264	R
61	28	M	2633	6	O	M+N	168	42	0.8	3108	Y	132	R
62	39	M	3273	6	O	M	286	24	0.9	2976	N	264	R
63	40	M	3291	4	I	M+N	110	30	0.8	2174	Y	132	E
64	27	M	3296	5	O	M	123	25	1	1176	Y	288	R
65	34	F	3727	4	O	M+N	134	22	1	3124	N	48	R
66	64	M	4206	6	O	M+N	142	20	0.9	2961	Y	324	E
67	29	F	4218	2	O	M	92	24	1.1	3873	N	108	R
68	24	M	4323	3	O	M+N	104	22	0.8	2844	Y	240	E
69	38	M	4537	4	O	M+N	112	30	1	2679	Y	180	R

70	31	F	4706	4	O	M+N+C	108	26	0.9	2092	Y	276	E
71	22	M	5335	3	O	M	106	24	1.2	1876	N	168	R
72	23	M	5889	4	O	M	124	25	1	2174	N	180	R
73	33	M	5631	2	I	M+N	174	24	0.9	3968	N	60	R
74	21	M	5996	5	O	M	98	20	0.9	847	N	264	R
75	47	F	6340	4	O	M	160	22	1	2940	N	192	R
76	16	M	6888	4	O	M+N	110	32	1	5184	Y	168	R
77	41	M	7051	3	O	M+N	94	20	1	2646	Y	288	E
78	25	F	7152	6	O	M+N	114	24	1.1	2772	N	112	R
79	43	F	7388	4	O	M+N+C	120	22	1	2862	Y	180	E
80	34	M	7921	3	O	M	126	20	0.9	1203	N	96	R
81	18	M	8344	6	O	M	102	24	0.7	3563	N	132	R
82	28	M	8734	10	O	M	96	22	1.1	2364	N	216	R
83	19	F	9096	4	O	M+N	112	24	1.4	1081	Y	168	E
84	55	M	10592	3	O	M+N+C	176	20	1.3	2918	Y	168	R
85	32	M	11187	3	I	M+N+C	124	24	1	2471	Y	216	E
86	37	F	11190	6	O	M	94	22	1	3949	N	132	R
87	24	M	13150	8	O	M+N	152	20	0.8	2621	Y	216	R
88	29	F	13250	5	O	M+N	92	26	0.9	2084	Y	192	R
89	25	M	13678	4	O	M	132	22	0.8	3764	N	96	R
90	23	M	13885	4	O	M	126	26	1.1	6056	N	24	R
91	52	M	13990	6	O	M+N	194	24	1.2	2768	Y	132	R
92	34	F	14911	3	O	M	98	30	0.8	5805	N	180	R
93	42	M	15886	2	I	M	164	20	0.8	3186	N	228	R
94	25	M	16842	5	O	M+N	110	22	1.1	2681	N	108	R
95	32	M	17324	4	O	M+N	94	26	0.9	3212	Y	144	R
96	29	M	17315	6	O	M	114	24	1	2976	N	156	R
97	39	F	18225	6	O	N+C	120	28	1	2049	Y	168	E
98	34	M	18335	9	O	M+N	186	28	1.2	1672	Y	228	R
99	59	F	19028	3	O	M+N	102	20	1	2848	Y	348	E
100	21	M	19112	4	O	M+N	96	28	0.9	2216	Y	336	E

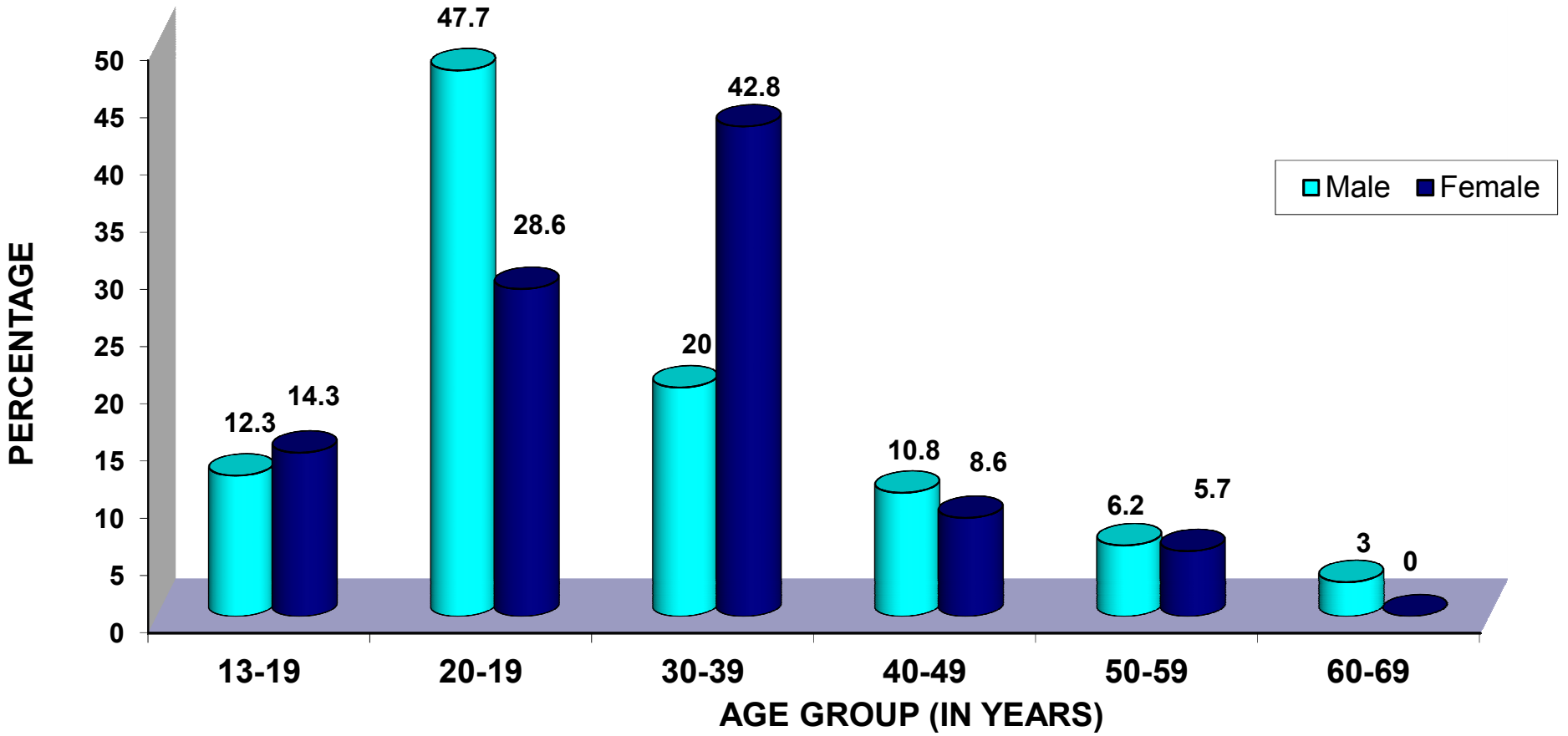
O – Oral I – Inhalation Y-Yes N – No R – Recovered E – Exposure

M - Muscarinic N - Nicotinic C- Central nervous system features

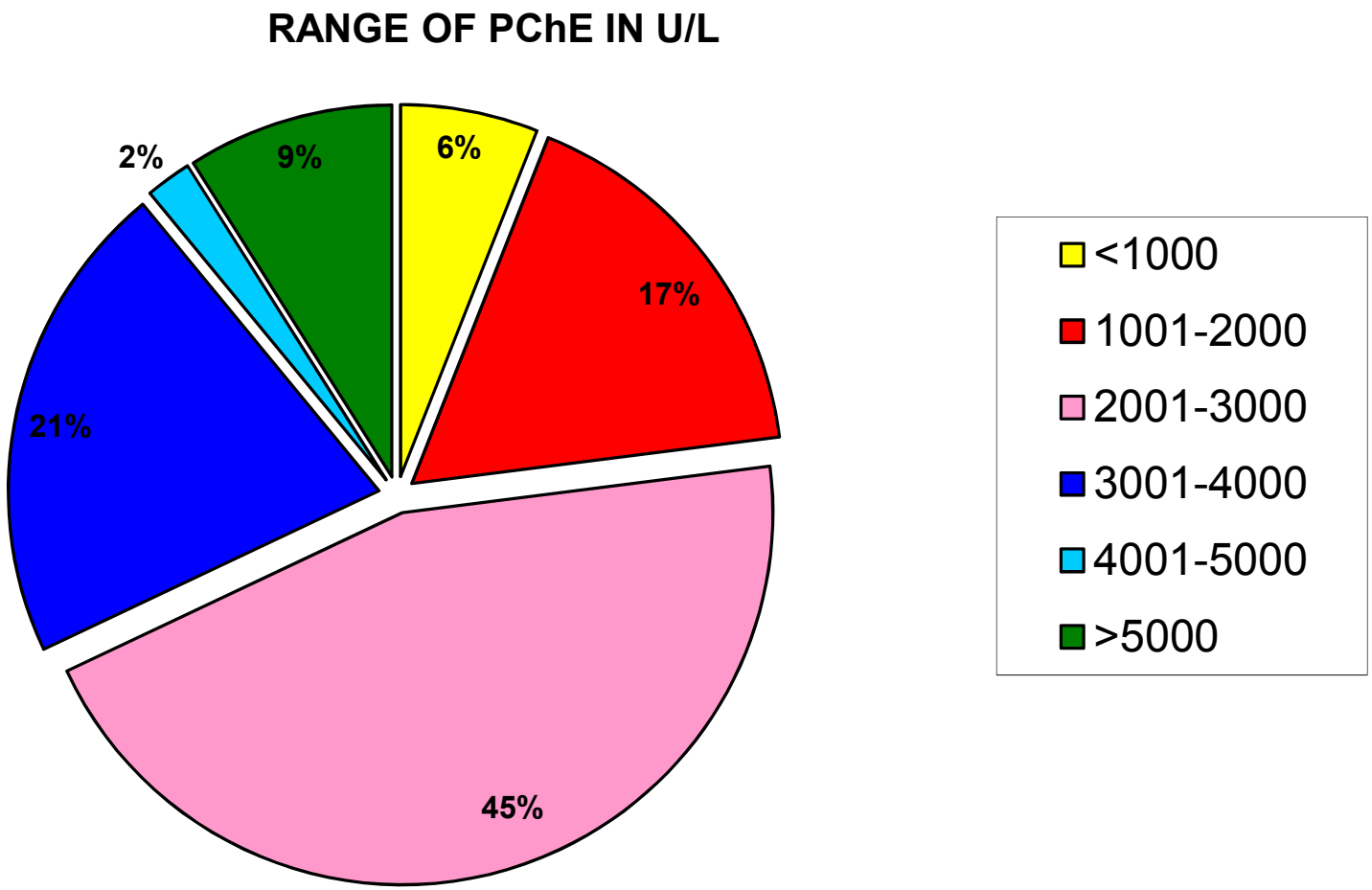
ABBREVIATIONS USED IN THIS BOOK

1. OP – Organophosphate
2. AChE – Acetyl Cholinesterase
3. PChE – Pseudo Cholinesterase
4. PAM – Pralidoxime
5. U/L – Units / Litre

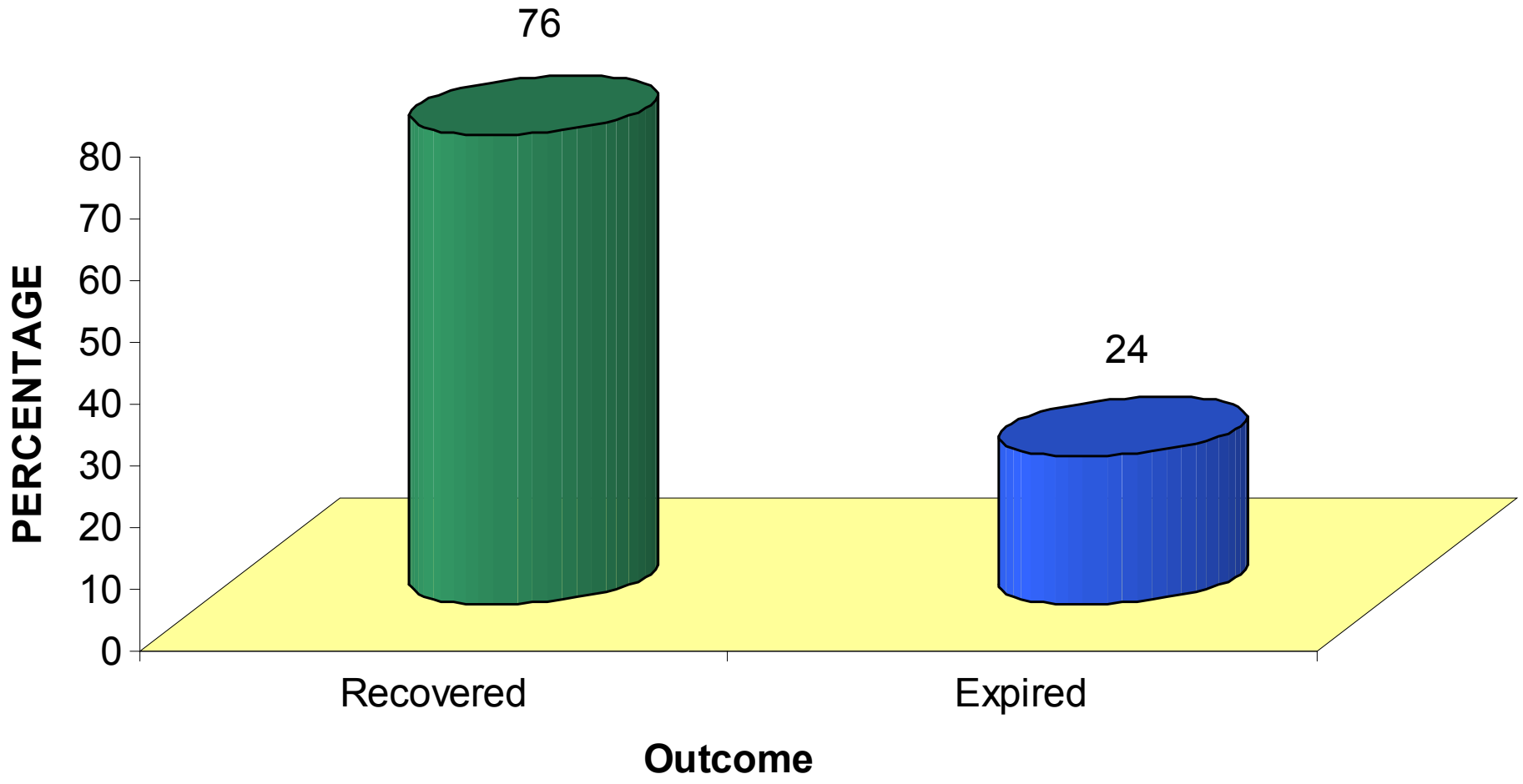
AGE-SEX DISTRIBUTION



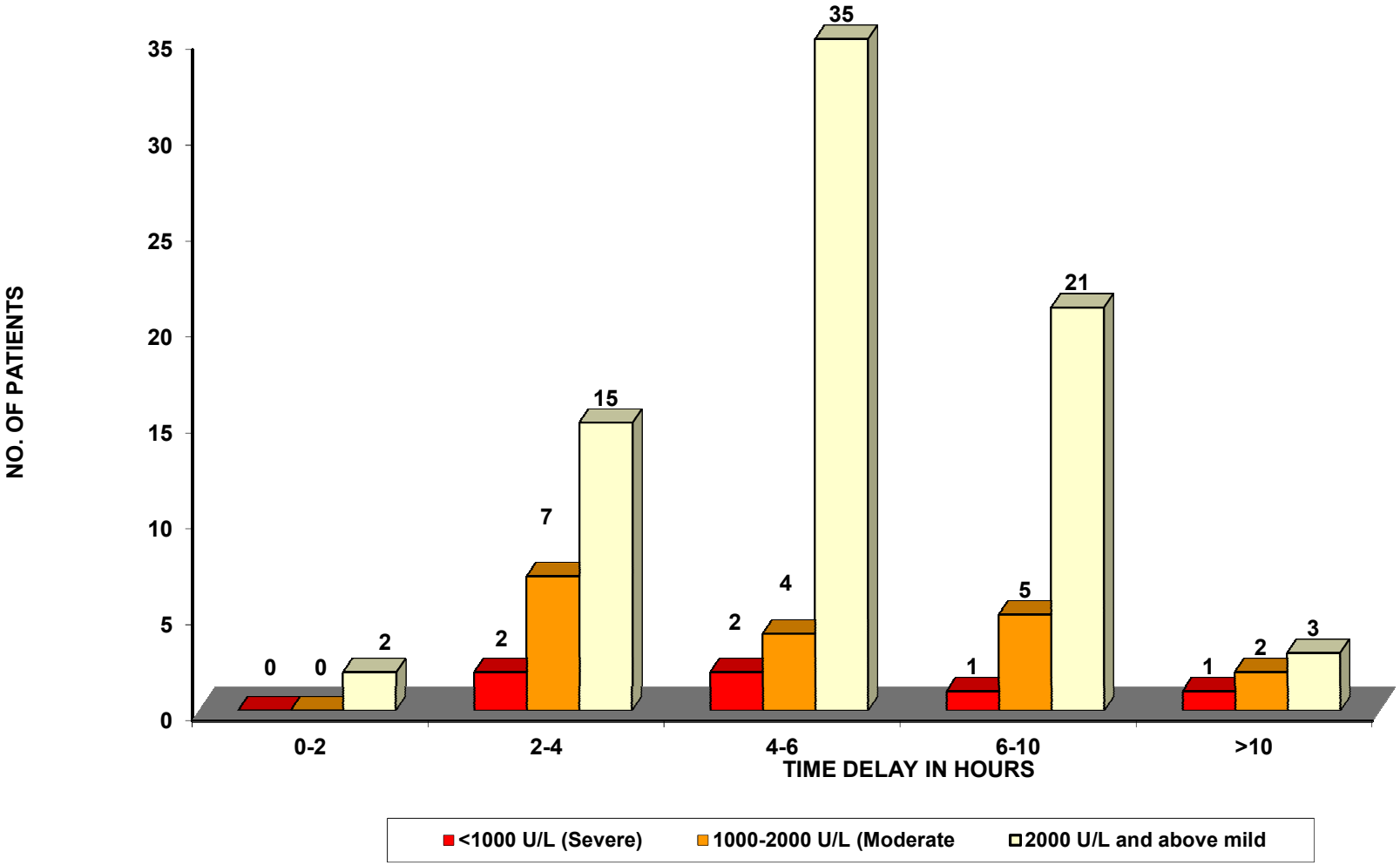
RANGE OF PSEUDOCHOLINESTERASE LEVELS AMONG PATIENTS



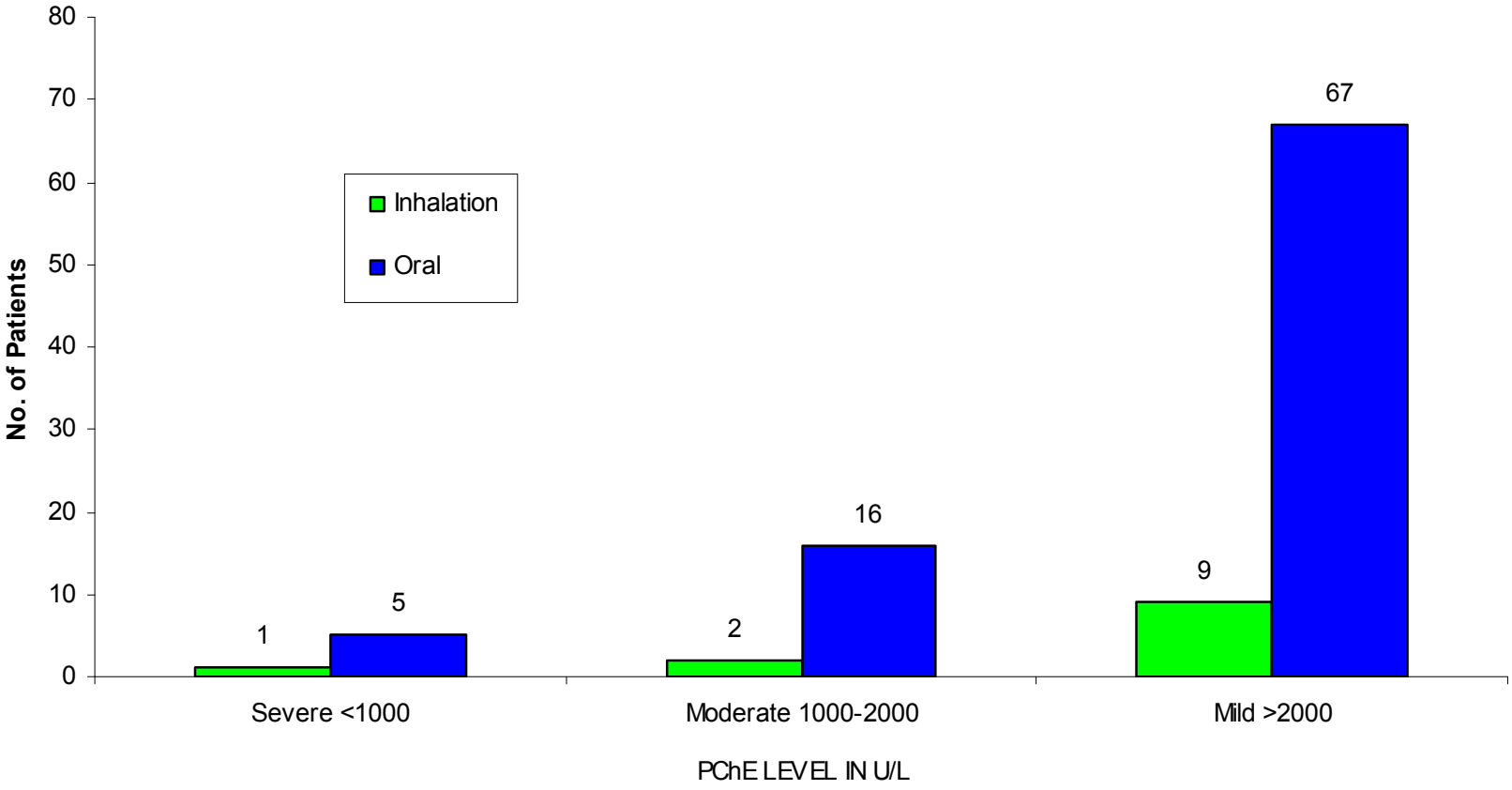
PERCENTAGE OF RECOVERED AND EXPIRED PATIENTS



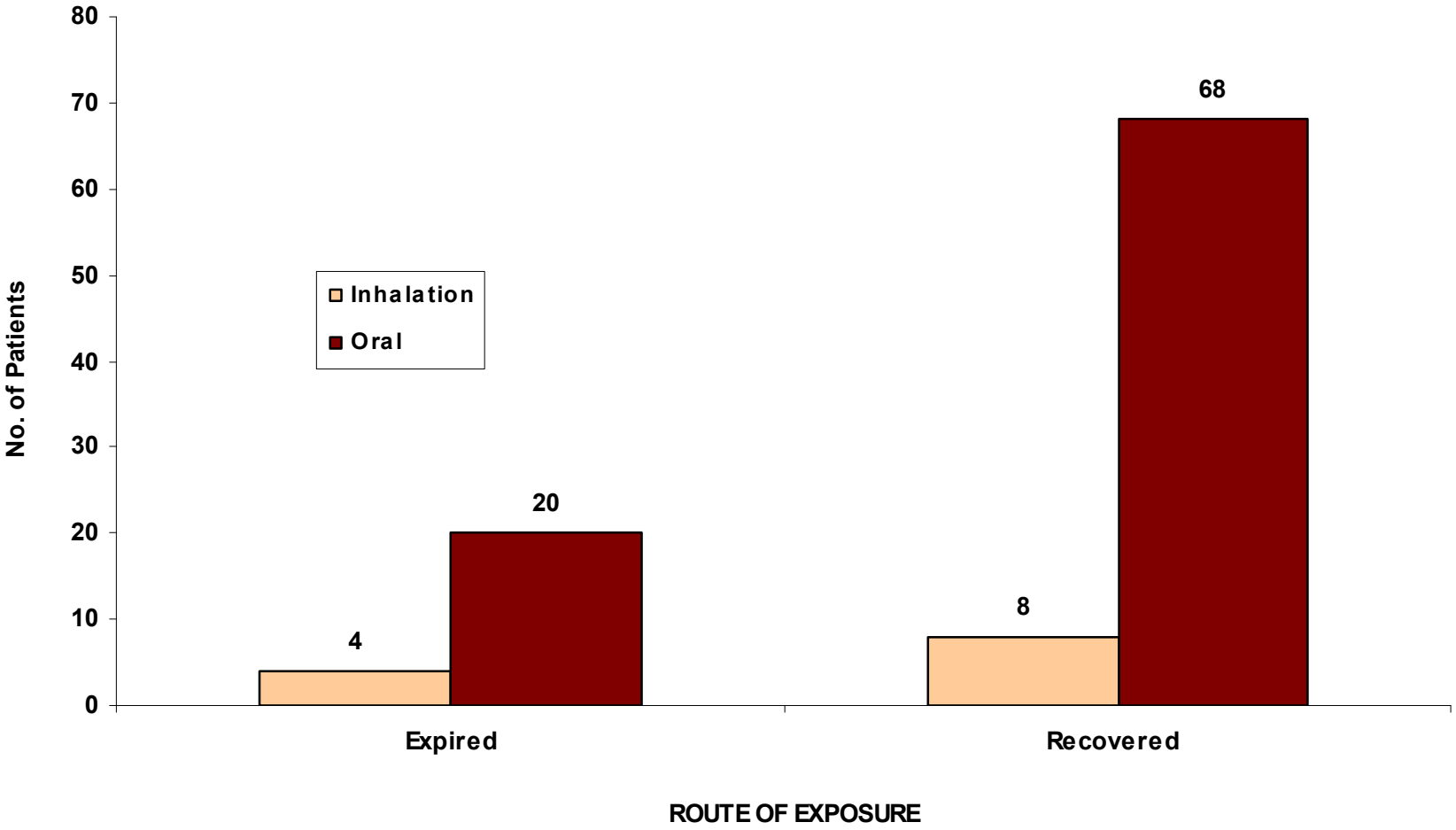
COMPARISION OF TIME DELAY WITH PChE LEVEL



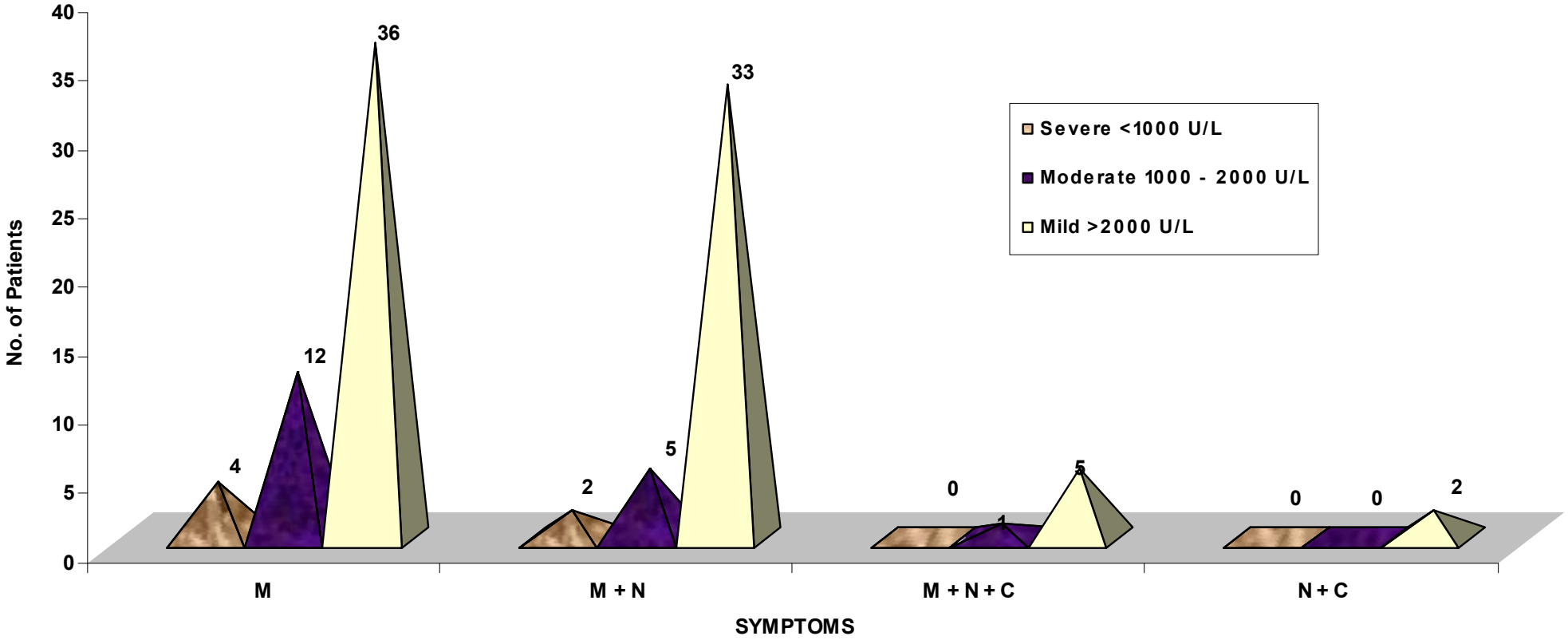
COMPARISION OF ROUTE OF EXPOSURE WITH PChE LEVEL



RELATION BETWEEN ROUTE OF EXPOSURE AND OUTCOME



SYMPTOMS RELATED WITH PChE LEVEL



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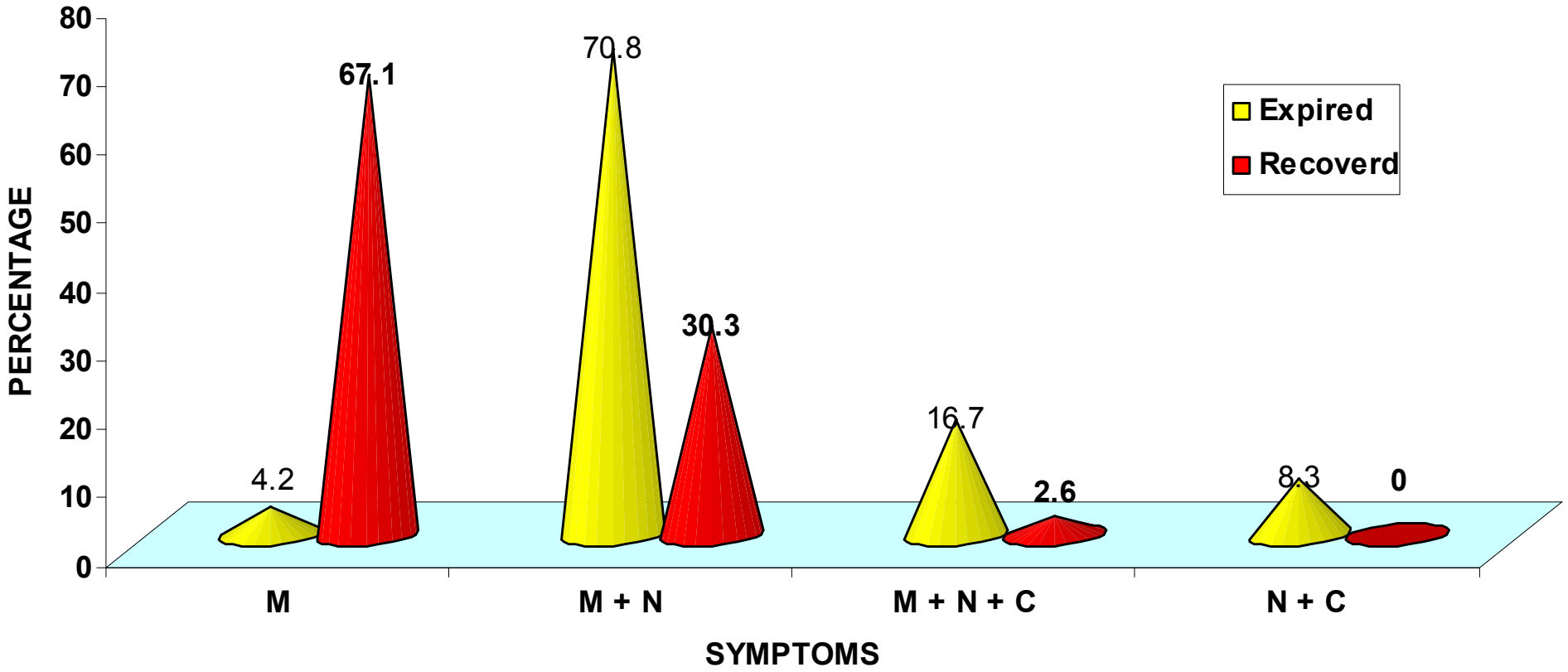
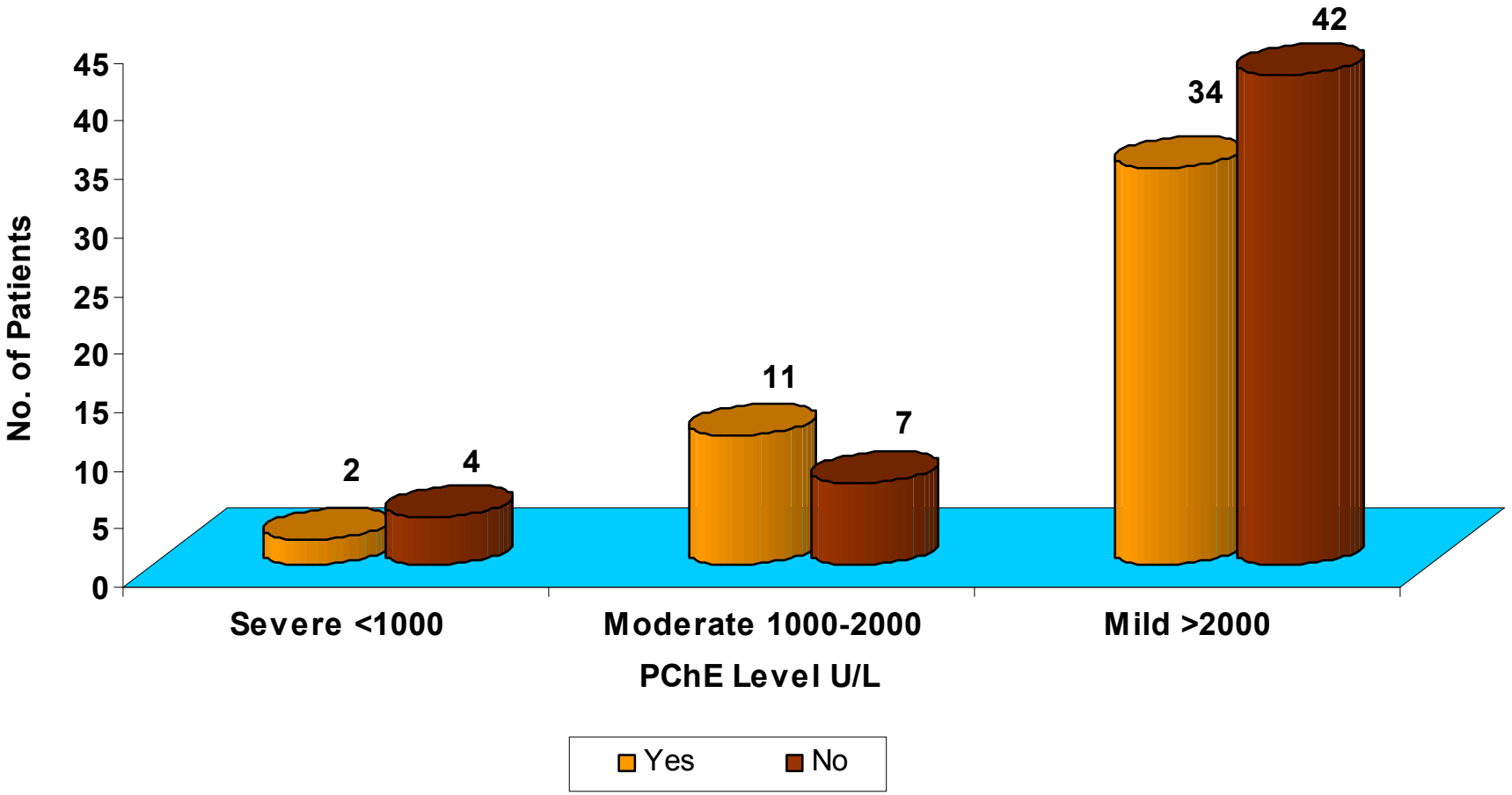
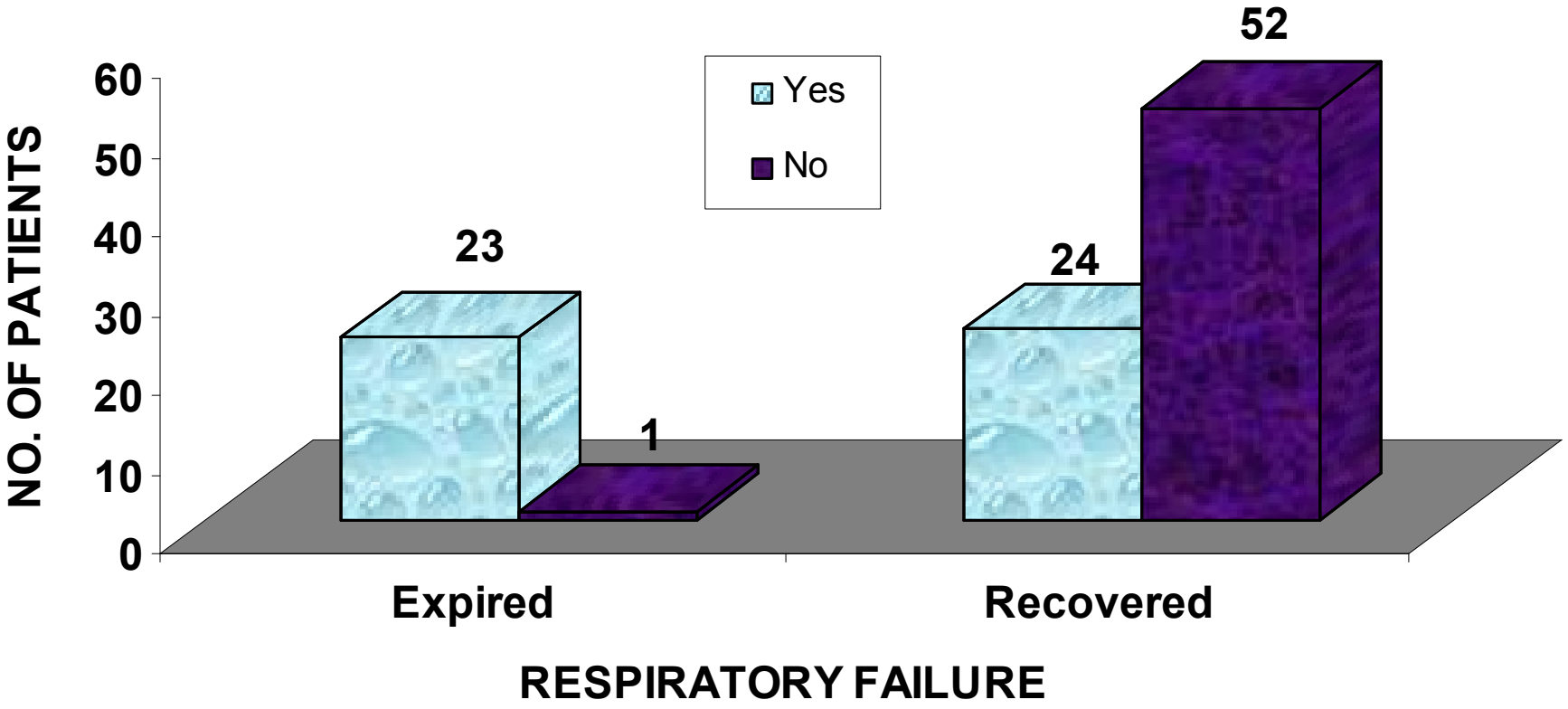


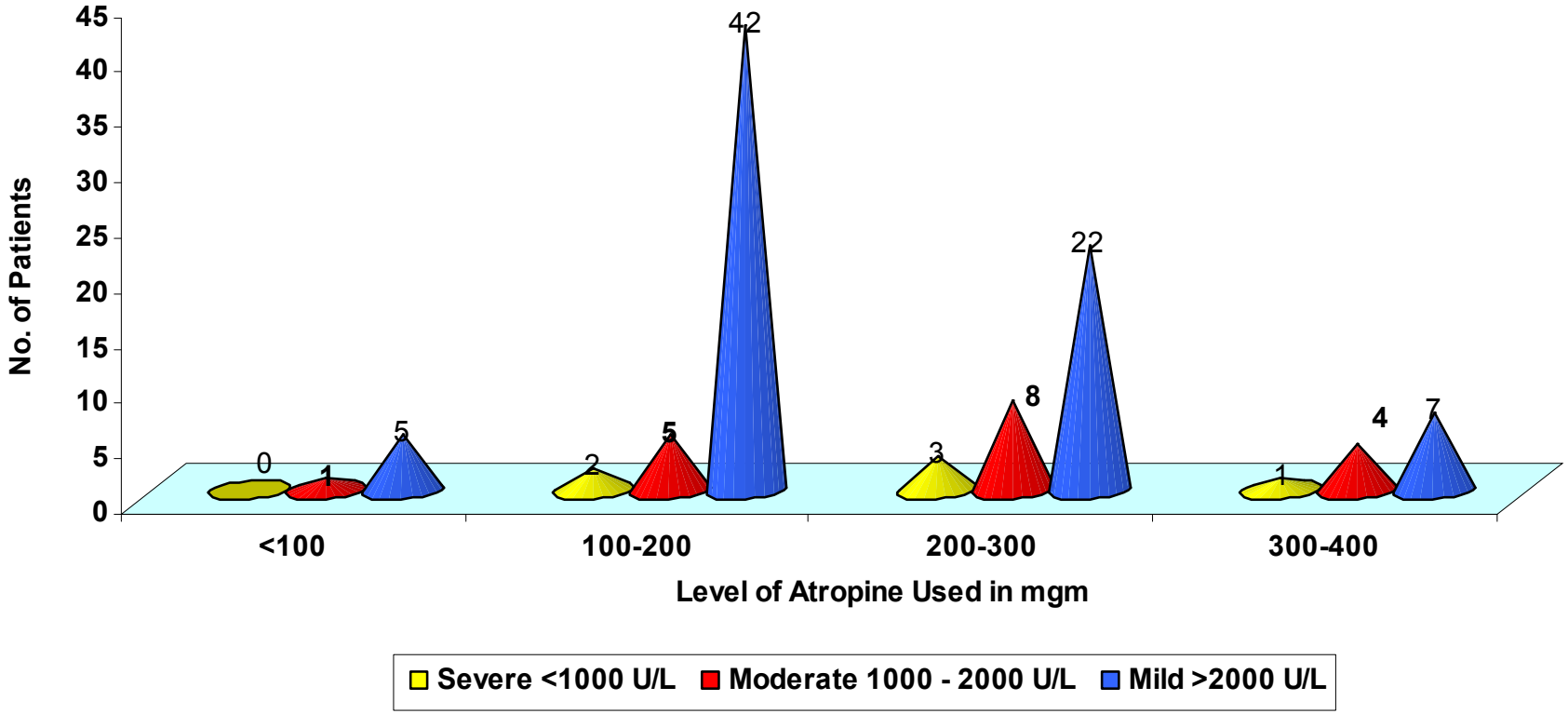
ASSOCIATION OF RESPIRATORY FAILURE WITH PChE LEVEL



RELATIONSHIP BETWEEN RESPIRATORY FAILURE WITH THE OUTCOME OF PATIENTS



ASSOCIATION BETWEEN ATROPINE REQUIREMENT WITH PChE LEVEL



CORRELATION BETWEEN ATROPINE REQUIREMENT AND OUTCOME